

Received: 2018.06.30  
Accepted: 2018.08.27  
Published: 2019.01.18

# Tracheobronchopathia Osteochondroplastica: A Case Report Illustrating the Importance of Multilevel Workup Clinical, Endoscopic and Histological Assessment in Diagnosis of an Uncommon Disease

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Statistical Analysis C  
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**Conflict of interest:** None declared  
**Source of support:** Internal funding, Department of Pathology, Central Hospital of Bolzano

**Patient:** Male, 62  
**Final Diagnosis:** Tracheobronchopathia osteochondroplastica  
**Symptoms:** Cough  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Pulmonology





**Objective:** Rare disease  
**Background:** Tracheobronchopathia osteochondroplastica (TO) is a rare idiopathic disease with a stable course, which involves the lumen of the tracheobronchial tree. Clinical manifestations at time of presentation may differ, typically including hoarseness, persistent and/or productive cough, hemoptyses, and dyspnea. There are no well-established guidelines for diagnostic workup and treatment. Our aim here is to present a paradigmatic case of TO together with a concise survey of the most important clinical, radiological, and histological criteria.

**Case Report:** We report a case of a 62-year-old non-smoker male with persisting cough and no prior history of respiratory disease. Chest radiography (RX) and computed tomography (CT) were unremarkable. Given the persistence of symptoms, the patient underwent bronchoscopic examination, which revealed protruding sessile nodules into the tracheal lumen, with cobblestone appearance. Histopathological examination of biopsies taken during bronchoscopy showed cartilaginous and osseous submucosal nodules consistent with the diagnosis of TO.

**Conclusions:** TO is not always an easily recognized disease, and a multidisciplinary team work is often required for diagnosis, with particular importance of endoscopic-pathological correlation.

**MeSH Keywords:** Bronchoscopy • Osteochondrodysplasias • Tracheal Diseases

**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/911859>

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## Background

TO is an uncommon disease of unknown etiology, characterized by the formation of multiple cartilaginous or osseous submucosal nodules that grow into the tracheobronchial lumen [1] TO is a rare benign disease with usually indolent but sometimes slowly progressive course and is characterized by the presence of multiple rock-garden-like nodules on bronchoscopy [1]. The disease was originally described in 1857 by Wilks, who reported autoptic findings of a number of bony plates in a 38-year-old man who died of tuberculosis [2]. The detection rate ranges from 1: 400 (0.25%) to 3: 1000 (0.30%) in autopsies and 1: 125 (0.80%) to 1: 10000 (0.01%) at bronchoscopy, with approximately 400 cases reported in the literature [3–6]. Some patients present problems with intubation when undergoing surgery [7,8]. Children and people younger than 50 years old only rarely have TO [9]. Most patients are asymptomatic and the disease is frequently diagnosed incidentally during intubation or endoscopy [10]. Chronic dyspnea on exertion is the most frequent symptom at the time of diagnosis. Others symptoms include chronic cough, hemoptysis, chest pain, and constitutional symptoms. Abnormal findings on chest auscultation are wheezing, stridor, and crackles [5]. The etiology of TO is still unclear and there are no standard diagnostic and treatment guidelines [11].

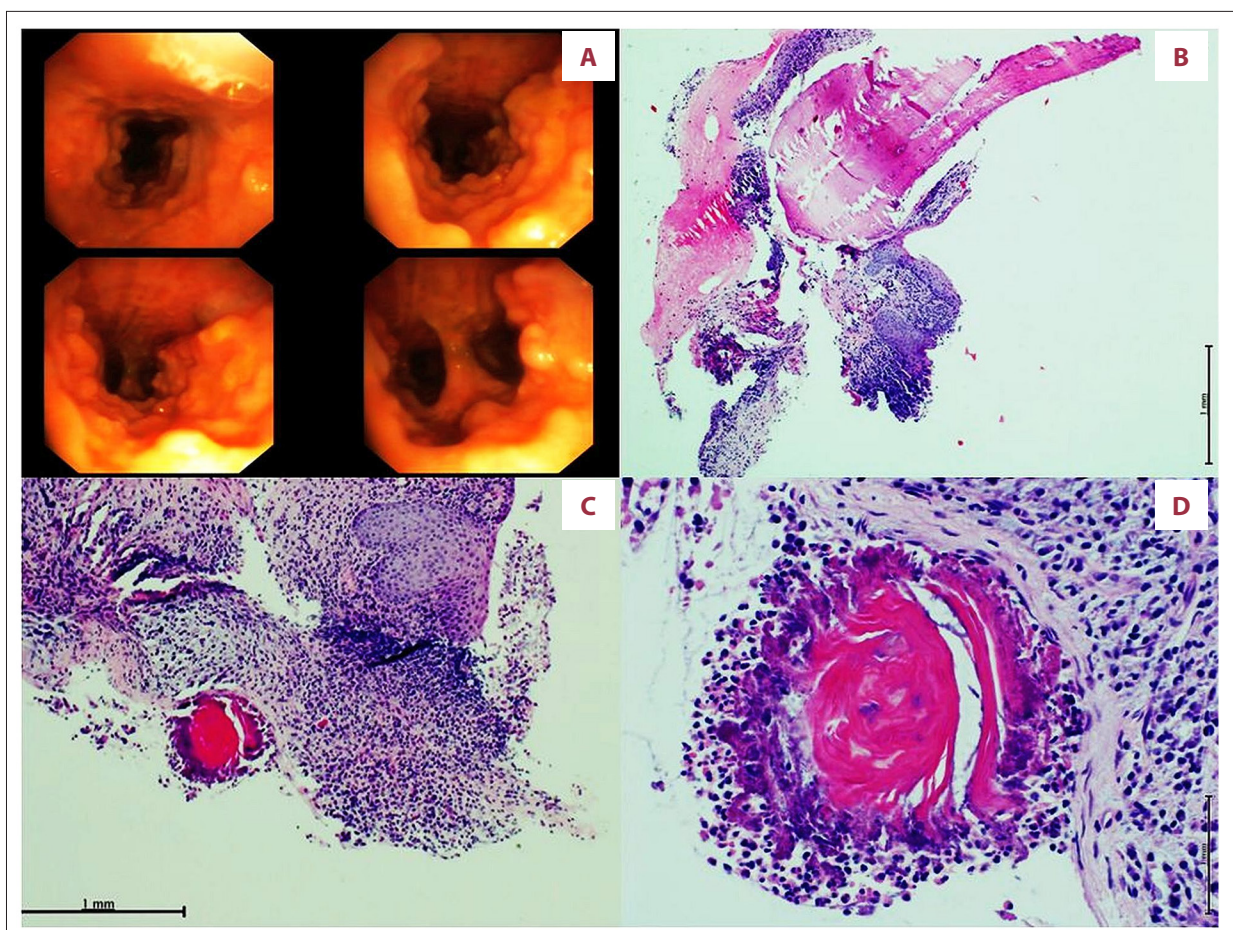
## Case Report

A 62-year-old, non-smoker male with a 2-month history of non-productive cough and hoarseness was admitted to the Respiratory Medicine Department of St. Maurizio Hospital-Bolzano. Clinically, coughing had started to occur more frequently in the last 2 weeks prior to admission, despite treatment with salmeterol/fluticasone (25/250 µg twice daily). History of allergies was unknown and there was no significant abnormality on physical examination. RX and thoracic CT scan were performed and were both unremarkable. Persistence and worsening of symptoms led to perform a fiberoptic bronchoscopy (FOB) examination to exclude a process of neoplastic nature, which was the initial main differential diagnosis considered. FOB showed sessile nodules, partly conglomerated, protruding into the tracheobronchial lumen, with a so-called “rock garden” or “cobblestone” appearance. The nodules gave a typical gritty sensation while passing the scope through the narrowed lumen. Notably, the posterior membranous tracheal wall was spared, with a regular appearance of the mucosa. The rigidity of the airway wall and the presence of these hard nodules hinder advancing the scope (Figure 1A). During bronchoscopy, many biopsy samples of the nodules were taken. Grossly, the samples represented 6 minimal grayish fragments measuring 0.3 to 0.6 cm. Histopathological examination showed diffuse erosions of the respiratory epithelium with extensive

foci of squamous metaplasia. In the underlying submucosa we found multiple and well-developed cartilaginous and osseous nodules, intermingled with chronic infiltration of inflammatory cells, mainly lymphocytes and histiocytes. Some calcified nodules showed an unusual elongated morphology, suggesting a possible connection with the perichondrium of the tracheal rings (Figure 1B). Other nodules were more similar to a central island of osteocytes, without any connection with nearby structures (Figure 1C, 1D). The histological features, in accordance with clinical and endoscopic data, were consistent with the final diagnosis of TO.

## Discussion

TO is a rare benign disease of unknown etiology characterized by the formation of multiple cartilaginous or osseous nodules in the submucosal layer of the trachea or larger bronchi. Typical bronchoscopic appearance consists in so-called “rock-garden” nodules protruding into the airway lumen. In particular, due to lack of cartilage in the posterior wall of the airway tree, these nodules typically involve the antero-lateral walls of the trachea and bronchus. The disease is currently listed under the osteochondrodysplasia category and ecchondrosis and exostosis proposed by Virchow in 1869 and metaplasia of the elastic tissue by Aschoff in 1910 have been the 2 main theories aiming to explain the origin and pathogenesis of the lesion [12,13]. A study by Tajima et al. has showed that bone morphogenetic protein-2 (BMP-2) and transforming growth factor beta-1 (TGF-beta 1) are potent inducers of new bone formation. Positive BMP-2 immunoreactivity was detected in numerous mesenchymal cells and chondroblasts lining the nodules in the tracheal submucosa. BMP-2 plays an important role in nodule formation and acts synergistically with TGF-beta 1 to promote the nodule induction cascade in the tracheal submucosa [14]. Others have previously suggested that undifferentiated connective tissue cells situated in the submucosal and elasticity layer transformed to cartilage and bone [15,16]. TO can be an incidental finding at autopsy or a diagnosis late in life. Due to very slow progression and the non-specificity of the symptoms [17,18], TO can long be misinterpreted as allergy or asthma [19]. Nowadays, due to improvements of diagnostic tools, most cases present as an incidental finding during clinic-radiological investigations [11]. Recently, new endoscopic techniques have been proposed to increase detection of subtle mucosal changes associated with TO [20]. According to the typical bronchoscopic visualization and to the histopathologic exam, TO can be divided into 3 stages: Stage I (early stage, mild grade), Stage II (middle stage, moderate grade), and Stage III (late stage, severe grade) [11]. CT is usually the best non-invasive method for evaluation of tracheobronchial lesions [21]. Findings on CT scans usually show calcified nodular densities protruding into the tracheal



**Figure 1.** (A) Multiple sub-mucosal nodules protruding into the tracheal lumen with typical “rock garden” or “cobblestone” appearance. The posterior membranous tracheal wall is spared. (B) An ossified nodule with unusual elongated morphology. Prominent squamous metaplasia of the respiratory epithelium and the chronic inflammatory elements are clearly recognizable. Original magnification, 40 $\times$ . (C) An ossified nodule configuring a central island of osteocytes. Original magnification, 100 $\times$ . (D) Higher magnification of an ossified nodule. Original magnification, 200 $\times$ .

lumen, with an abnormally irregular tracheal morphology and decreased lateral diameter [7,22]. In our case, initial imaging investigations did not indicate diagnosis of the disease, and subtle alterations in general imaging were considered within normal limits, as sometimes reported [4,19]; therefore, bronchoscopic examination was necessary. The role of bronchoscopy is important for the differential diagnosis because other diseases, such as amyloidosis, relapsing polychondritis, tracheobronchomalacia, tracheobronchial papillomatosis, and, most important, neoplastic process of the airways, can present with similar features [3]. A key feature of TO in bronchoscopic differential diagnosis with other diseases with nodular appearance such as amyloidosis, papillomatosis, polychondritis, and sarcoidosis is the characteristic sparing of the posterior wall of the trachea [23]. Histopathological examination remains the fundamental step to ensure a proper diagnosis [24]. Biopsies usually show erosion of respiratory epithelium, squamous metaplasia, and multiple and well-developed cartilaginous and

osseous nodules in the underlying submucosa, together with variable inflammatory infiltration. Also, in our case, given the history of recently-presenting cough and the absence of an allergic background, the primary point in differential diagnosis was to exclude a process of neoplastic nature, and the biopsy clearly showed features of the disease.

Diagnosis of TO is made on the basis of endoscopy, CT scan, and histopathology, highlighting the need for a multidisciplinary approach [3,10,22,25]. There is no consensus for treatment of this rare disease, and most therapies are palliative, focusing on the symptoms. Possible treatments include endoscopic excision, laser ablation, surgical resection, and even radiotherapy [26–28]. Patients with TO presenting with acute breathlessness can show rapid resolution of symptoms by administration of inhaled beclomethasone dipropionate and budesonide [7]. Severe cases of TO, such as those complicated by significant airway stenosis or recurrent obstructive infection,



should be managed with other options, including laser ablation and surgical resection. When significant airway obstruction is present, endoscopic removal of the lesions seems to be the treatment of choice [16,29,30]. However, most reports suggest that the disease has a very indolent course, and many patients have stable symptoms for many years [17,18]. For this reason, and to avoid unnecessary treatments, it is important to be aware of the existence of this condition and of its characteristic features, keeping in mind that a single diagnostic tool could be insufficient to establish a reliable diagnosis, which can be better achieved with multidisciplinary workup.

## Conclusions

TO is a rare idiopathic disease with a stable or indolent course, that involves the lumen of the tracheobronchial tree. Clinical

mimickers and absence of consensus about treatment make diagnosis and subsequent appropriate treatment challenging. As in our case, an easy and rapid diagnosis cannot be achieved with minimal investigation, and a multidisciplinary approach, especially using histopathological examination of biopsies, is key to accurate diagnosis of this rare disease.

## Department and Institution where work was done

Department of Respiratory Medicine, St. Maurizio Hospital, Bolzano; the Department of Pathology, Central Hospital of Bolzano; and the Department of Pathology and Diagnostics, University and Hospital Trust of Verona, Verona.

## Conflicts of interest

None.

## References:

1. Uchimura K, Yamasaki K, Yatera K et al: Multiple tracheobronchial polypoidosis caused by tracheobronchopathia osteochondroplastica. *Intern Med*, 2016; 55: 3165–67
2. Lundgren R, Stjernberg NL: Tracheobronchopathia osteochondroplastica. A clinical bronchoscopic and spirometric study. *Chest*, 1981; 80: 706–9
3. Jindal S, Nath A, Neyaz Z, Jaiswal S: Tracheobronchopathia osteochondroplastica – a rare or an overlooked entity? *J Radiol Case Rep*, 2013; 7: 16–25
4. Sun J, Xie L, Su X, Zhang X: Tracheobronchopathia osteochondroplastica: Case report and literature review. *Respir Med Case Rep*, 2015; 15: 14–17
5. Jabbaridjani HR, Radpey B, Kharabian S, Masjedi MR: Tracheobronchopathia osteochondroplastica: Presentation of ten cases and review of the literature. *Lung*, 2008; 186: 293–97
6. Prakash UBS: Tracheobronchopathia osteochondroplastica. *Semin Respir Crit Care Med*, 2002; 23: 167–76
7. Tadjeddein A, Khorgami Z, Akhlaghi H: Tracheobronchopathia osteoplastica: Cause of difficult tracheal intubation. *Ann Thorac Surg*, 2006; 81: 1480–82
8. Matsuki T, Takeda Y, Kida H, Kumanogoh A: Tracheobronchopathia osteochondroplastica: A cause of difficult tracheal intubation. *Intern Med*, 2018; 57: 909–10
9. Simsek PO, Ozelik U, Demirkazik F et al: Tracheobronchopathia osteochondroplastica in a 9-year-old girl. *Pediatr Pulmonol*, 2006; 41: 95–97
10. Laine M, Sanaa E, Fouad K, JEB: Tracheobronchopathia osteochondroplastica associated with skin cancer: A case report and review of the literature. *BMC Res Notes*, 2014; 7: 637
11. Zhu Y, Wu N, Huang HD et al: A clinical study of tracheobronchopathia osteochondroplastica: Findings from a large Chinese cohort. *PLoS One*, 2014; 9: e102068
12. Toth C: [Tracheopathia osteoplastica. A 100-year-old mystery]. *Pathologe*, 2012; 33: 129–34 [in German]
13. Ashley DJ: Bony metaplasia in trachea and bronchi. *J Pathol*, 1970; 102: 186–88
14. Tajima K, Yamakawa M, Katagiri T, Sasaki H: Immunohistochemical detection of bone morphogenetic protein-2 and transforming growth factor beta-1 in tracheopathia osteochondroplastica. *Virchows Arch*, 1997; 431: 359–63
15. Smid L, Lavrenck B, Zargi M: Laryngo-tracheo-bronchopathia chondro-osteoplastica. *J Laryngol Otol*, 1992; 106: 845–48
16. Zack JR, Rozenshtein A: Tracheobronchopathia osteochondroplastica: Report of three cases. *J Comput Assist Tomogr*, 2002; 26: 33–36
17. Brandén E: A 20-year follow-up of a case with tracheobronchopathia osteochondroplastica. *J Bronchology Interv Pulmonol*, 2013; 20: 84–86
18. Leske V, Lazor R, Coetmeur D et al: Tracheobronchopathia osteochondroplastica: A study of 41 patients. *Medicine (Baltimore)*, 2001; 80: 378–90
19. Fois AG, Arcadu A, Santoru L et al: Tracheobronchopathia osteochondroplastica: A rare case report of a non-smoker and non-atopic patient, with a long history of wheezing since childhood. *Multidiscip Respir Med*, 2016; 11: 16
20. Ihara H, Tajima K, Yoshikawa H et al: Autofluorescence imaging bronchoscopy as a novel approach to the management of tracheobronchopathia osteochondroplastica: A case report. *J Thorac Dis*, 2016; 8: E1195–98
21. Acar T, Bayraktaroglu S, Ceylan N, Savas R: Computed tomography findings of tracheobronchial system diseases: A pictorial essay. *Jpn J Radiol*, 2014; 33: 51–58
22. Devaraja K, Sagar P, Chirom AS: Tracheobronchopathia osteochondroplastica: Awareness is the key for diagnosis and management. *BMJ Case Rep*, 2017; 2017: pii: bcr-2017-220567
23. Nielsen SW, Stevens JR, Dion GR, Howard NS: Dyspnea, dysphonia, and cough: Varied presentations of tracheobronchopathia osteochondroplastica. *Ann Otol Rhinol Laryngol*, 2015; 124: 829–33
24. Abu-Hijleh M, Lee D, Braman SS: Tracheobronchopathia osteochondroplastica: A rare large airway disorder. *Lung*, 2008; 186: 353–59
25. Wang N, Long F, Jiang S: Tracheobronchopathia osteochondroplastica two cases reports and review of literature. *Med (United States)*, 2016; 95: e3396
26. Nienhuis DM, Prakash UB, Edell ES: Tracheobronchopathia osteochondroplastica. *Ann Otol Rhinol Laryngol*, 1990; 99: 689–94
27. Gleich LL, Rebeiz EE, Pankratov MM et al: YAG Laser-assisted otolaryngologic procedures. *Arch Otolaryngol Neck Surg*, 1995; 121: 1162–66
28. Kanat F, Teke T, Ozer F: Tracheopathia osteoplastica associated with iron deficiency anemia. *Indian J Chest Dis Allied Sci*, 2005; 47: 47–51
29. Danckers M, Raad RA, Zamuco R et al: A complication of tracheobronchopathia osteochondroplastica presenting as acute hypercapnic respiratory failure. *Am J Case Rep*, 2015; 16: 45–49
30. Sood N, Khandelvia BK, Bugnait G: Tracheobronchopathia osteochondroplastica: An unusual presentation with near total occlusion of airways. *Indian J Pathol Microbiol*, 2016; 59: 129–30